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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,759	09/19/2005	Ignacio Blanco Blanco	034284-003	6945

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BUCHANAN INGERSOLL PC
(INCLUDING BURNS, DOANE, SWECKER & MATHIS)
POST OFFICE BOX 1404
ALEXANDRIA, VA 22313-1404

EXAMINER	
HAMIDINIA, SHAWN A	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 05/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/549,759	BLANCO, IGNACIO BLANCO	
	Examiner	Art Unit	
	Shawn Hamidinia	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/27/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Priority

1. The current application filed on September 19, 2005 claims priority of Spanish application 200402282/5 filed on September 24, 2005.

Information Disclosure Statement

2. The information disclosure statement filed on January 27, 2006 has been considered. Please see the attached initialed PTO-1449.

Claim Rejections - 35 USC § 112 and § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claims 1-5 provide for the use of alpha-1 antitrypsin, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 1-5 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 2, 8 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 2 the applicant uses the phrase "other therapeutic forms". It is unclear as to what the applicant is claiming to be the invention. This phrase has not been discussed, explained or defined anywhere in the specification.

Claims 8 and 10 recite the limitation "or at a risk of developing". This phrase has not been explained or defined in the specification and it is completely unclear how one would know if a person is at risk of developing fibromyalgia. Claims 9 and 11-13 are also rejected as being dependent from rejected claims 8 and 10 and failing to cure the defect.

Claim Rejections - 35 USC § 112, First Paragraph-Written Description

8. Claims 8 and 10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 8 and 10 are directed to a method of treatment comprising administering alpha-1 antitrypsin to a patient suffering from, or at risk of developing, fibromyalgia by increasing the alpha-1 antitrypsin levels by 100% or 5-fold greater than the basal levels for a given period of time.

The specification does not provide any representative examples of a person "at a risk of developing" fibromyalgia encompassed by this claim. A review of the full content of the specification indicates that patients were first diagnosed with fibromyalgia before

treatment began. However, there is no description of how to determine if an individual is at risk for developing fibromyalgia. As such, the specification fails to provide sufficient descriptive information for the method of treating individuals by administering alpha-1 antitrypsin. There is no description of what constitutes a patient who is at risk for developing fibromyalgia. Also, there is no disclosure of when treatment should begin if that information was available.

Applicants are not in possession of a method of treating patients "at risk of developing fibromyalgia" because the specification is devoid of teachings of how to determine if a patient is at risk. Given this lack of disclosure, Applicants' written description of the claimed invention is insufficient to show that Applicants were in possession of the full scope of the claimed invention.

Claim Rejections - 35 USC § 112-Enablement

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 8 and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for a method of treatment comprising administering sufficient alpha-1 antitrypsin to an individual at risk of developing fibromyalgia. The specification does not enable any person skilled in the art

to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404).

Factors to be considered in determining whether a disclosure would require undue experimentation include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In the instant case, (1) the amount of experimentation is large because studies must be carried out to: a) determine the risk factors for developing fibromyalgia, b) measuring the AAT serum levels in each individual. Measuring the AAT serum levels in each individual requires a great deal of resources and such a massive study is

necessary to ascertain with no uncertainty all those who are at risk of developing fibromyalgia. (2) Also, there is no guidance provided by the specification on how to determine those who are at risk of developing fibromyalgia. The specification does not describe how to determine who is at risk of developing fibromyalgia and whether administering AAT to individuals at risk of developing fibromyalgia will effectively treat them. Further, (3) the specification is totally devoid of any working examples other than patients who are already suffering from fibromyalgia; As for the next Wands factor, (4) the nature of the invention is a method of treatment comprising administering AAT to people at risk of developing fibromyalgia. There is no prior art (5) which suggests how one could determine everyone at risk of developing fibromyalgia; (6) the relative level of skill in this art is very high; (7) the predictability of the art is low with regard to the determination of who is at risk of developing fibromyalgia. Finally, (8) the claims are extremely broad because every person in the world has some risk of developing fibromyalgia, rendering the claims undefined and uncharacterized.

Based on this analysis, the conclusion that it would require undue experimentation to practice the instant invention is inescapable.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-3 and 5-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Stoller et al. (2002).

Stoller et al. teach augmentation therapy for patients with severe deficiency of alpha-1 antitrypsin (AAT) by IV infusion of purified AAT to raise serum levels above the protective threshold of 80 mg/dL, (see paragraph 1, page 66). Stoller et al. also teach that the U.S. Food and Drug Administration approved this augmentation therapy in 1989 with a pasteurized pooled human plasma product, (see paragraph 1, page 66). Stoller et al. further teach that the infusion of pasteurized pooled human plasma AAT at a weekly dose of 60 mg/kg has been shown to raise serum levels of AAT and to maintain nadir levels above the protective threshold, (see paragraph 1, page 66).

13. Claims 1-3 and 5-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Juvelekian et al. (2004).

Juvelekian et al. teach that the specific pharmacological treatment of alpha-1 antitrypsin (AAT) deficiency is with AAT augmentation, (see paragraph 2, page 1743). Juvelekian et al. also teach that currently available drugs achieve augmentation of serum AAT levels by intravenous infusion of purified pooled human plasma AAT, (see paragraph 2, page 1747). Juvelekian et al. further teach that AAT is produced and secreted from the hepatocyte into the bloodstream, where normal serum levels range between 100-350 mg/dL, depending on the individual laboratory, (see paragraph 3,

page 1744). Jevelekian et al. also teach that based on epidemiological studies regarding the prevelance of emphysema with various phenotypic variants of AAT, the protective threshold has been identified as approximately 80 mg/dL, (see paragraph 3, page 1744).

On page 7 of the instant application, Table 1 lists the levels of AAT (mg/dL) in the serum of three patients who were diagnosed with fibromyalgia. All three patients had basal serum AAT levels ranging from 40- 93 mg/dL, which are all lower than the normal serum level ranges as taught by Juvelekian et al. Table 1 further shows that after 7 days, symptoms of fibromyalgia disappeared and this correlated with serum AAT levels ranging from 71-209 mg/dl.

Jevelekian et al. teach administering 60 mg/kg of purified AAT obtained from pooled plasma from healthy donors once weekly, (see paragraph 4, page 1748). Jevelekian et al. teach that subjects with AAT deficiency received this drug weekly for up to 26 weeks and an immediate sharp rise in serum AAT levels (>300 mg/dL) was followed by a decline, (see paragraph 4, page 1748). Jevelekian et al. teach that a 4-fold sustained increase in the AAT levels were observed. Jevelekian et al. teach another administration study with 4-weekly infusions of purified pooled human plasma AAT at a concentration of 250 mg/kg. Finally, Jevelekian et al. teach the administration of 120 mg/kg of purified pooled human AAT to patients by infusion, (see paragraph 1, page 1749).

14. Claims 1-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Döring et al. (1999).

Döring et al. teach that alpha-1 antitrypsin deficiency is one of the most common disorders among white populations with autosomal recessive heredity, (see paragraph 1, page 363). Döring et al. further teach that individuals suffering from AAT deficiency were treated by intravenous administration with **recombinant** alpha-1 antitrypsin, (see left column, lines 23-24, page 369). Döring et al. teach weekly infusions of 60-94 mg/kg plasma-derived alpha-1 antitrypsin to AAT deficient individuals, (see paragraph 2, page 369).

Conclusion

15. No claims are allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shawn Hamidinia whose telephone number is (571) 272-4534. The examiner can normally be reached on Mon-Fri from 9:00 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SAH

ROBERT A. WAX
PRIMARY EXAMINER